REMARKS

Claims 62-63, 65-66, 68-69, 76-77, 79 and 89-141 are pending in this application. Applicant has cancelled claims 76-77, 79, 104, 113, 115, 118, 120, and 129-141 without prejudice. Applicant fully reserves the right to prosecute the subject matter of canceled claims 76-77, 79, 104, 113, 115, 118, 120, and 129-141 in one or more related applications.

Applicant has also amended claims 62-63, 65-66, 68-69, 90-94, 97-103, 105, 107-109, 111-112, 114, 116-117, 119, 121-122, and 124-128 and added new claims 142-192 to clarify certain embodiments of the present invention. Specifically, claims 62-63, 65-66, 68-69, 90-94, 97-103, 105, 107-109, 111-112, 114, 116-117, 119, 121-122, and 124-128 have been amended for clarification purposes. Support for new claims 142-192 can be found in the specification as follows:

New Claim(s)	Support in Specification
142	"a combination of said isolated Tat protein, fragment and mutant" (original claims 1-6)
143	"for inducing an immune response" (page 1, line 31 to page 2, line 3; page 8, lines 15-17; page 9, lines 17-22; page 15, lines 16-18; page 16, lines 3-6; page 17, lines 4-14; page 42, lines 4, 6, and 17; page 50, lines 15-17; page 70, lines 13-14; page 71, lines 3-6; page 101, lines 9-10; page 107, lines 14-17; and Example 4)
144, 145,	"purified" (page 10, line 18; page 25, lines 7-8 and 25; page 26, line 9; page 42, lines 8-9; and page 50, lines 13-14)
146	"the ability of [a biologically active] isolated Tat protein, fragment or mutant to (iii) activate virus replication . . . in cells transfected with a HIV-1 promoter-reporter plasmid" (page 14, line 31 to page 15, lines 1-2; page 15, lines 7-10; and original claims 2 and 4)
147	"wild type Tat protein" (page 1, line 6; page 14, lines 19-21 and 29-30; and original claim 58)
148, 150	"purified" (page 10, line 18; page 25, lines 7-8 and 25; page 26, line 9; page 42, lines 8-9; and page 50, lines 13-14)
149	"SEQ ID NO. 2" (page 37, lines 1-10; and original claims 42 and 43)
151	"adjuvant" (page 11, lines 27-28; page 16, lines 27-30; and original claim 26)
152	"administration is intradermal" (page 17, line 15; and original

	claim 37)
153	"administration is subcutaneous" (page 17, line 15; and original claim 37)
154	"Alum" (original claims 27 and 59)
155	"the ability of [a biologically active] isolated Tat protein, fragment or mutant to "(i) become internalized by activated endothelial cells or dendritic cells . . . by fluorescence microscopy; and" (page 28, lines 14-15 and 24-27; and page 33, line 30 to page 34, line 1) "(ii) activate the proliferation, migration, and invasion of Kaposi's sarcoma (KS) cells or cytokine-activated endothelial cells in culture . . . at a concentration of up to 1 μg/ml; and" (page 14, line 31 to page 15, lines 1-2; page 15, lines 5-6; and original claims 1 and 4) "(iii) activate virus replication . . . in cells transfected with a HIV-1 promoter-reporter plasmid" (page 14, line 31 to page 15, lines 1-2; page 15, lines 7-10; and original claims 2 and 4)
156	"wild type Tat protein" (page 1, line 6; page 14, lines 19-21 and 29-30; and original claim 58)
157, 159	"purified" (page 10, line 18; page 25, lines 7-8 and 25; page 26, line 9; page 42, lines 8-9; and page 50, lines 13-14)
158	"SEQ ID NO. 2" (page 37, lines 1-10; and original claims 42 and 43)
160	"adjuvant" (page 11, lines 27-28; page 16, lines 27-30; and original claim 26)
161	"administration is intradermal" (page 17, line 15; and original claim 37)
162	"administration is subcutaneous" (page 17, line 15; and original claim 37)
163	"Alum" (original claims 27 and 59)
164, 179	"comprises the cysteine rich region of Tat" (page 2, lines 22-23) "in a non-oxidated form" (page 24, lines 21-25; and original claim 56)
165-168, 173, 178	"in a non-oxidated form" (page 24, lines 21-25; and original claim 56)

169, 174	"Tat mutant" (page 1, line 6; page 10, line 18; page 16, lines 10-14; and original claim 58)
170, 172, 175, 177	"purified" (page 10, line 18; page 25, lines 7-8 and 25; page 26, line 9; page 42, lines 8-9; and page 50, lines 13-14)
171, 176	"SEQ ID NO. 7" (page 37, lines 11-20; original claims 44 and 45)
180	"wild type Tat protein" (page 1, line 6; page 14, lines 19-21 and 29-30; and original claim 58)
181, 183	"purified" (page 10, line 18; page 25, lines 7-8 and 25; page 26, line 9; page 42, lines 8-9; and page 50, lines 13-14)
182	"SEQ ID NO. 2" (page 37, lines 1-10; and original claims 42 and 43)
184	"adjuvant" (page 11, lines 27-28; page 16, lines 27-30; and original claim 26)
185	"administration is intradermal" (page 17, line 15; and original claim 37)
186	"administration is subcutaneous" (page 17, line 15; and original claim 37)
187	"Alum" (original claims 27 and 59)
188	"T-helper peptide or T-helper universal epitope of Tetanus Toxoid" (page 10, lines 15-20; page 28, lines 11-13; and original claim 12)
189	"HIV rev, nef or gag, or an immunogenic fragment thereof" (Abstract, lines 4-5; page 1, lines 7-8; page 5, lines 20-24; page 10, lines 15-24; and original claim 13)
190	"an immuno-modulant cytokine" (Abstract, line 5; page 6, lines 27-30; page 10, lines 15-29; and original claim 15)
191	"IL-12 or IL-15" (Abstract, line 5; page 6, lines 27-30; page 9, lines 12-17; page 10, lines 25-29; and original claim 16)
192	"Tat mutant" (page 1, line 6; page 10, line 18; page 16, lines 10-14; and original claim 58) "SEQ ID NO. 7" (page 37, lines 11-20; original claims 44 and 45) "administration to a human" (page 10, lines 15-16)

No new matter has been added. Upon entry of the present amendments, claims 62-63, 65-66, 68-69, 89-103, 105-112, 114, 116-117, 119, 121-128 and 142-192 will be pending in the present application.

I. THE CLAIM REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

The rejection of claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 106-107, 115, 120, 128-129, 133 and 137 under 35 U.S.C. § 102(b) ("Section 102(b)") as allegedly being anticipated by Chang *et al.* (AIDS. 1997 Oct;11(12):1421-31, "Chang") is maintained by the Examiner. Specifically, the Examiner alleges that the limitation "in a form suitable for administration to a human" is an intended use and does not put a specific structural limitation on the composition. For the following reasons, Applicant respectfully disagrees.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. W.L. Gore Associates v. Garlock, Inc., 721 F.2d 1540, 1554 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984); In re Donohue, 766 F.2d 531 (Fed. Cir. 1985). To anticipate a patent claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. MEHL/Biophile International Corp. v. Milgraum, 192 F.3d 1362 (Fed. Cir. 1999); In re Robertson, 169 F.3d 743 (Fed. Cir. 1999). It is well established that in order for a prior art reference to amount to an inherent anticipation of a claim, all the elements of the claim must necessarily, inevitably, and always result from the prior art disclosure and would be so recognized by one of ordinary skill in the art; mere possibilities or probabilities are not sufficient. *See* Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1269, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991); W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1553-54, 220 U.S.P.Q. 303, 313-14 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984); In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 325-26 (C.C.P.A. 1981); Phillips Petroleum Co. v. U.S. Steel Corp., 673 F.Supp. 1278, 1295 n.12, 6 U.S.P.Q.2d 1065, 1076-77 n.12 (D. Del. 1987), aff'd, 865 F.2d 1247, 9 U.S.P.Q.2d 1461 (Fed. Cir. 1989); Hughes Aircraft Co. v. U.S., 8 U.S.P.Q.2d 1580, 1583 (Ct. Cl. 1988); Ex parte Levy, 17 U.S.P.Q.2d 1461, 1463-64 (B.P.A.I. 1990); Ex parte Skinner, 2 U.S.P.Q.2d 1788, 1788-89 (B.P.A.I. 1987). As stated by the Court of Appeals for the Federal Circuit:

> we are not persuaded that the 'effect' of the processes disclosed in [the prior art patents], an 'effect' undisclosed in those patents, would be always to inherently produce or be seen always to produce products meeting all of the claim limitations.

> Anticipation of inventions set forth in product claims cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.

W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1554, 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (citing In re Felton, 484 F.2d 495, 500, 179 U.S.P.Q. 295, 298 (C.C.P.A. 1973)).

Claim 62 has been amended herein to clarify that the claimed composition, which comprises the isolated, biologically active Tat protein, mutant, or fragment, is in a form suitable for administration to a human. Applicant respectfully disagrees with the Examiner's construction of the term "suitable for administration to a human" as meaning a composition that will not kill the human recipient (see Office Action, page 3, lines 14-17). Applicant submits that one of skill in the art would construe the term "suitable for administration to a human" in the context of the teachings of the specification as meaning that the composition meets the safety criteria for human administration put forth by regulatory agencies such as the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA) which have the public responsibility for determining whether substances are suitable for human administration. Thus, the compositions suitable for administration to a human are not construed merely as those that will not kill the intended recipient. As evidence of the foregoing, provided herewith is a Declaration of Shayne Gad, Ph.D. under 37 C.F.R. § 1.132 ("Gad Declaration"). Dr. Gad, an expert in toxicology and issues relating to development and approval of biologics, states that, in his opinion, the term "suitable for administration to a human" means that the composition is sufficiently safe for administration to human patients using the criteria for safety defined by regulatory agencies such as the FDA and the EMEA. Gad Decl. ¶2.

Applicant submits that Chang does not teach or suggest each and every element of amended claim 62 and thus, its dependent claims. In particular, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, in a form suitable for administration to a human, as recited in amended claim 62.

Chang discloses two methods for Tat purification, *i.e.*, (1) a first method involving high-pressure liquid chromatography (HPLC) and ion-exchange chromatography (see Chang, page 1424, left column, under section entitled "Tat protein and anti-Tat antibody"); and (2) a second method involving heparin affinity chromatography (see Chang, page 1424, left column, under section entitled "Purification of recombinant Tat protein by heparin affinity

chromatography"). Applicant submits that the Tat proteins obtained by both methods are neither inherently nor explicitly disclosed by Chang to be suitable for administration to a human, as recited in amended claim 62. Specifically, regarding the first method, which is silent regarding the solvent used in the HPLC method, the resulting Tat preparation is not necessarily suitable for use in human and thus does not meet the standard for inherent anticipation. Regarding the second method, the isolated Tat protein is tainted with chemicals that are not suitable for administration to a human. The resulting composition would not be one meeting the safety criteria of regulatory agencies such as the FDA and the EMEA. This is discussed in more detail below.

By citations to reference 18 and 44, Chang indicates that the first method is carried out as described in two prior publications, Ensoli *et al.* ("Release, uptake, and effects of extracellular human immunodeficiency virus type 1 Tat protein on cell growth and viral transactivation." J Virol. 1993 Jan;67(1):277-87, hereinafter "Ensoli"), and Bohan *et al.* ("Analysis of Tat transactivation of human immunodeficiency virus transcription in vitro." Gene Expr. 1992;2(4):391-407, hereinafter "Bohan"), a copy of each of which is enclosed as Exhibits 3 and 4, respectively, to the Gad Declaration. A review of Ensoli and Bohan shows that the Tat protein obtained by the first method was expressed in *E. coli* and isolated by successive rounds of HPLC and ion-exchange chromatography (see Ensoli, page 278, left column, under section entitled "Tat protein and anti-Tat antibodies," lines 1-4). The purified Tat protein was then lyophilized in the presence of 0.1 mM dithiothreitol (DTT), and suspended, before use, in degassed phosphate buffered saline (PBS) (containing 0.1% bovine serum albumin (BSA) (containing 2.67 mM potassium chloride, 137.93 sodium chloride, 1.47 mM potassium phosphate monobasic, and 8.06 mM sodium phosphate dibasic), added with 0.1 mM DTT and 0.1% (weight/volume) BSA to prevent loss of Tat biological activity (see Ensoli, page 278, left column, under section entitled "Tat protein and anti-Tat antibodies," lines 7-13). For each procedure involving the use of Tat or Tat-containing supernatants, the plastic ware was rinsed previously in PBS-BSA or RPMI medium containing 10% fetal calf serum (FCS), respectively, to avoid protein loss by adsorption on the plastic (see Ensoli, page 278, left column, under section entitled "Tat protein and anti-Tat antibodies," lines 13-16).

In the first method, the HPLC step was "reverse-phase" (see Bohan, page 393, right column, under section entitled "Purified Tat specifically transactivates HIV-1 in vitro," line 4). Although not explicitly stated in Chang, Ensoli, or Bohan, one skilled in the art would understand that in each complete round, HPLC was performed after the ion-exchange chromatography, and thus, the eluted Tat protein would be tainted with HPLC buffer. In

support thereof, provided herewith is a Declaration of Barbara Ensoli, M.D., Ph.D. Under 37 C.F.R. § 1.132 ("Ensoli Declaration") which explains the foregoing in ¶5. Dr. Ensoli, the inventor of this application, states that one of ordinary skill in the art would have understood that the HPLC step would have been performed after the ion-exchange chromatography step since one skilled in the art would know that HPLC preferably is not performed on crude bacterial extracts, and since the skilled artisan also would have been aware that a reverse-phase fractionation was desirable after ion-exchange in order to facilitate removal of ion-exchange buffer salts. Ensoli Decl. ¶5.

Applicant points out that Chang and its cited references do not indicate the solvent used for reverse phase HPLC. Since Chang does not explicitly teach that the solvent is one that results in a Tat preparation suitable for administration to human, the first Tat purification method taught by Chang does not explicitly anticipate the claimed invention. Moreover, the first Tat purification method also cannot anticipate under the doctrine of inherency since it is not inevitable that a solvent was used that results in a Tat preparation suitable for administration to a human. See W.L. Gore & Assocs., Inc. v. Garlock, Inc., *supra.*

A common solvent for reverse phase HPLC is acetonitrile, usually also containing trifluoroacetic acid (TFA). The Examiner's attention is invited to the Ensoli Declaration at ¶5, which evidences the foregoing. Since the first method described in Chang is silent as to the identity of the solvent used in the HPLC, Chang is thereby silent as to the nature of any contaminants in the Tat preparation resulting therefrom. Therefore, in order for the resulting Tat composition to anticipate the claimed invention, the Tat composition must inevitably be suitable for human administration, under the standards enunciated by the courts under the doctrine of inherency. However, applying the appropriate legal standard shows that the Tat produced by the first purification method of Chang cannot anticipate under the doctrine of inherency because it is not inevitably and necessarily suitable for administration to a human. See Ensoli Decl. ¶5. Indeed, if the common acetonitrile/TFA solvent combination were used (which it was), the Tat preparation would not be suitable for administration. The resulting Tat preparation would not be suitable for administration to a human, since it would have contained traces of acetonitrile and TFA.

Specifically, neither acetonitrile nor TFA are suitable for administration to a human. As Dr. Gad sets forth in his Declaration, acetonitrile and TFA are very toxic both acutely and upon repeat exposure and both are mutagens. Gad Decl. ¶5. Levels of acetonitrile in therapeutics are very restricted, and TFA is not recognized as an allowed pharmaceutical ingredient in any form. In addition, since TFA is a mutagen and a teratogen, it would not be

allowed in the production process of any therapeutic. Gad Decl. ¶5. As such, these solvents should be avoided in any production process for a therapeutic and would not be used in any production process where they might appear as a detectable impurity. Gad Decl. ¶5. Accordingly, Dr. Gad concludes that compositions of Tat purified using acetonitrile and TFA as solvents would not be suitable for administration to a human. Gad Decl. ¶5.

Moreover, with respect to the Tat preparation that is used in Chang to produce rabbit polyclonal antibodies, Chang indicates that the Tat preparation used for this method was obtained by the first purification method, discussed above, under the heading of Chang entitled "Tat protein and anti-Tat antibody," since the paragraph regarding production of antibodies appears under this heading. Thus, the Tat preparation used for production of polyclonal antibodies does not anticipate the claims, because it is not explicitly or inherently disclosed by Chang to be suitable for administration to a human, for all the reasons discussed above.

Like the first method, the second Chang method also expressed Tat in *E. coli*, followed by sonication in 40 ml of lysis buffer, which includes 20 mM sodium phosphate, 2.5% glycerol, 0.2 mM phenylmethylsulfonyl fluoride (PMSF), 5 mM DTT, 50 mM mannitol, 10 mM ascorbic acid, and 500 mM NaCl (see Chang, page 1424, left column, under section entitled "Purification of recombinant Tat protein by heparin affinity chromatography," lines 1-6). The lysate was then clarified by centrifugation and the supernatant was incubated at room temperature with 2 ml of heparin-sepharose prewashed with lysis buffer prior to packing into a glass column, where it was further washed with lysis buffer until no protein was detected in the wash (see Chang, page 1424, left column, under section entitled "Purification of recombinant Tat protein by heparin affinity chromatography," lines 8-14). The bound material was then eluted with lysis buffer containing 2 M NaCl (see Chang, page 1424, left column, under section entitled "Purification of recombinant Tat protein by heparin affinity chromatography," lines 14-16).

Thus, the Tat protein obtained by the second method is formulated with the disclosed lysis buffer which contains 0.2 mM PMSF. PMSF is a highly toxic compound. Gad Decl. ¶8. In fact, PMSF is not allowed as a pharmaceutical ingredient of any form and would not even be allowed in any process where it could be detected as an impurity. Gad Decl. ¶8. Since, in this second purification method disclosed by the Chang reference, PMSF is an actual component of the Tat composition, this composition would not be a composition suitable for administration to humans. Gad Decl. ¶8.

As detailed above and in the Gad Declaration, the compositions resulting from the two purification protocols disclosed in Chang would not be suitable for administration to a human. Thus, Applicant submits that claims 62, 63, 65, 66, 68, 69, 89-103, 105-128, 140, and 142-189, all of which require that the Tat composition be suitable for administration to a human, are novel over Chang. Withdrawal of the Section 102(b) rejection is respectfully requested.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103 ARE IN ERROR AND SHOULD BE WITHDRAWN

1. The Claims Are Patentable Over Chang in View of Heiman

The rejection of claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 106-107, 113-115, 118-120, 128-129, 133 and 135-137 under 35 U.S.C. § 103(a) ("Section 103(a)") as allegedly being obvious over Chang in view of the web pages entitled "HIV Vaccines: Where are we Going?" (http://www.niaid.nih.gov/daids/vaccine/1998nature.htm, "Heiman") is maintained by the Examiner. Specifically, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the protein of Chang with the antigens of Heiman with the expectation of at least an additive effect (see Office Action, page 8, lines 3-7). The Examiner also indicates that Heiman was not cited to teach a Tat protein but to teach that numerous combinations of HIV proteins are known in the art, including, specifically, gag.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Graham v. Deere, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. In re O'Farrell, 853 F.2d 894, 902-4 (Fed. Cir. 1988); In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. In re Dow Chemical Co., 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." Hartness International Inc. v. Simplimatic Engineering Co., 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987).

The deficiencies in the teaching of Chang are discussed above. Moreover, the presently claimed invention is not obvious over Chang. Chang teaches the preparation of Tat for production of antibodies in rabbits and for use in *in vitro* assays. Chang does not suggest that Tat is useful in therapeutic or prophylactic methods in humans. As such, there is no motivation based on Chang to produce a Tat composition that would be suitable for administration to a human.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Heiman does not cure the deficiency of Chang, because Heiman does not suggest producing a Tat preparation that is suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Heiman does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

2. The Claims Are Patentable Over Chang in View of Vogel

The rejection of claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-95, 97, 101-111, 115-117, 120-122, 128-129, 133 and 137-139 under Section 103(a) as allegedly being obvious over Chang in view of Vogel *et al.* (Vogel FR, Powell MF. 1995. A compendium of vaccine adjuvants and excipients. In: Powell MF, Newman MJ, editors. Vaccine design: The Subunit and Adjuvant Approach. Plenum, New York, "Vogel") is maintained by the Examiner. Specifically, the Examiner indicates that Vogel was not cited to teach Tat but to teach various antigen enhancing compounds. The Examiner also alleges that Applicant does not specifically indicate why widely effective immune modulators suitable for a wide range of antigens would not work with Tat as was asserted in the previous Office Action.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Vogel does not cure the deficiency of Chang, because Vogel does not suggest producing a Tat preparation that is suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Vogel does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

3. The Claims Are Patentable Over Chang in View of Castignolles

The rejection of claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 99, 106-107, 115, 120, 128-129, 133 and 137 under Section 103(a) as allegedly being obvious over Chang in view of Castignolles *et al.* (Vaccine. 1996 Oct;14(14):1353-60, "Castignolles") is maintained by the Examiner. Specifically, the Examiner alleges that Castignolles was not cited to teach Tat but to teach that nanoparticles have immunostimulating properties. The Examiner further alleges that Applicant does not specifically indicate why effective immune modulators suitable for antigens would not work with Tat as was asserted in the previous Office Action.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Castignolles does not cure the deficiency of Chang, because Castignolles does not suggest producing a Tat preparation that is suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Castignolles does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

4. The Claims Are Patentable Over Chang in View of Ramshaw

The rejection of claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 100, 106-107, 115, 120, 128-129, 133 and 137 under Section 103(a) as allegedly being obvious over Chang in view of Ramshaw *et al.* (J Immunol Methods. 1977;18(3-4):251-5, "Ramshaw") is maintained by the Examiner. Specifically, the Examiner alleges that Ramshaw was not cited to teach Tat but to teach that autologous erythrocytes are efficient at inducing an immune response. The Examiner further alleges that Applicant does not specifically indicate why erythrocytes would not work with Tat as was asserted in the previous Office Action.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Ramshaw does not cure the deficiency of Chang, because Ramshaw does not suggest producing a Tat preparation that is

suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Ramshaw does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

5. The Claims Are Patentable Over Chang in View of Livingston

Claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 106-107, 112, 115, 120, 128-129, 133 and 137 are rejected under Section 103(a) as allegedly being obvious over Chang in view of Livingston *et al.* (J Immunol. 1997 Aug 1;159(3):1383-92, "Livingston"). Specifically, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate the T cell helper epitope of tetanus toxin of Livingston to the Tat protein of Chang, finding motivation to enhance the immunogenicity of Chang's Tat protein.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Livingston does not cure the deficiency of Chang, because Livingston does not suggest producing a Tat preparation that is suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Livingston does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

6. The Claims Are Patentable Over Chang in View of Barry

Claims 62-63, 65-66, 68-69, 76-77, 79, 89-90, 93-94, 106-107, 115, 120, 123, 128-129, 133 and 137 are rejected under Section 103(a) as allegedly being obvious over Chang in view of Barry *et al.* (Clin Pharmacokinet. 1997 Mar;32(3):194-209, "Barry"). Specifically, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the addition of an antiviral composition in the composition to inhibit viral disease.

As discussed above, Chang does not teach or suggest a composition, which comprises an isolated, biologically active Tat protein, mutant, or fragment, that is in a form suitable for administration to a human, as recited in amended claim 62. Barry does not cure the

deficiency of Chang, because Barry does not suggest producing a Tat preparation that is suitable for administration to a human, and thus, does not provide the missing motivation. Accordingly, the combination of Chang plus Barry does not teach the presently claimed invention.

In view of the foregoing, Applicant respectfully submits that this Section 103(a) rejection is in error and respectfully requests the Examiner to withdraw the rejection.

II. INFORMATION DISCLOSURE STATEMENT FILED ON NOVEMBER 17, 2005

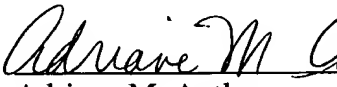
It has come to the attention of Attorneys for Applicant that the List of Related Art Cited by Applicant ("List") that was filed on November 17, 2005 has not been initialed by the Examiner and returned to Attorneys for Applicant. When Examiner Stucker was contacted on December 13, 2005 regarding this matter, the Examiner suggested that Applicant provide with the instant response a copy of the Information Disclosure Statement and List as filed, as well as a copy of the stamped postcard receipt, indicating the receipt by the PTO of these documents. The Examiner also requested that Attorneys for Applicant supplement their response in the future with a List of References Cited that provides the titles (which were omitted from the List). Applicant respectfully requests that the Examiner consider and make of record the references cited on the List. A copy of the Information Disclosure Statement and List as filed on November 17, 2000, with a copy of the stamped postcard receipt, are attached as Exhibit A.

CONCLUSION

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: December 13, 2005



32,605 (Reg. No.)

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Enclosures